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The Contents of Case 09848164

Qnum	Query	DB Name	Thesaurus	Operator	Plural
Q1	(rhode)[IN] OR (jiao)[IN]	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q2	(rhode)[IN] OR (jiao)[IN] or (burkhardt)[IN] or (wong)[in]	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q3	Q2 and MHC	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q4	(single adj chain) near (class adj II)	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q5	(single adj chain) same (class adj II)	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q6	Q5 not Q4	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q7	tetramer near MHC	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES

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(FILE 'HOME' ENTERED AT 15:54:07 ON 22 NOV 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 15:54:18 ON 22 NOV 2002

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L1          9889 S RHODE P?/AU OR JIAO J?/AU OR BURKHARDT ?/AU OR WONG H?/AU
L2            47 S L1 AND MHC
L3            22 DUP REM L2 (25 DUPLICATES REMOVED)
L4             9 S L3 AND (SINGLE (1N) CHAIN)
L5           128 S MHC AND (CLASS (1N) II)  AND (SINGLE (1N) CHAIN)
L6            21 S L5 AND PD<19960131
L7            10 DUP REM L6 (11 DUPLICATES REMOVED)
L8            10 S L7 NOT L4

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 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
 NEWS 16  Aug 08  CANCERLIT reload
 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
 NEWS 20  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03  JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16  Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA
 NEWS 27  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985
 NEWS 28  Oct 21  EVENTLINE has been reloaded
 NEWS 29  Oct 24  BEILSTEIN adds new search fields
 NEWS 30  Oct 24  Nutraceuticals International (NUTRACEUT) now available on STN
 NEWS 31  Oct 25  MEDLINE SDI run of October 8, 2002
 NEWS 32  Nov 18  DKILIT has been renamed APOLLIT

 NEWS EXPRESS  October 14 CURRENT WINDOWS VERSION IS V6.01,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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FILE 'HOME' ENTERED AT 15:54:07 ON 22 NOV 2002

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COST IN U.S. DOLLARS

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FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 15:54:18 ON 22 NOV 2002

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FILE 'BIOSIS' ENTERED AT 15:54:18 ON 22 NOV 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

=> s Rhode P?/au or Jiao J?/au or Burkhardt ?/au or Wong H?/au
L1 9889 RHODE P?/AU OR JIAO J?/AU OR BURKHARDT ?/AU OR WONG H?/AU

=> s l1 and MHC
L2 47 L1 AND MHC

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 22 DUP REM L2 (25 DUPLICATES REMOVED)

=> s l3 and (single (1N) chain)
L4 9 L3 AND (SINGLE (1N) CHAIN)

=> dis l4 1-9 ibib abgs
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=> dis l4 1-9 ibib abs

L4 ANSWER 1 OF 9 MEDLINE
ACCESSION NUMBER: 1999110189 MEDLINE
DOCUMENT NUMBER: 99110189 PubMed ID: 9894898
TITLE: Display of functional alphabeta **single-chain** T-cell receptor molecules on the surface of bacteriophage.
AUTHOR: Weidanz J A; Card K F; Edwards A; Perlstein E; **Wong H C**
CORPORATE SOURCE: Sunol Molecular, Miramar, FL 33025, USA.. jaweid@laker.net
CONTRACT NUMBER: R43-CA76856-01 (NCI)
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1998 Dec 1) 221 (1-2) 59-76.

Journal code: 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990129

AB The ability to display functional T-cell receptors (TCR) on the surface of bacteriophage could have numerous applications. For instance, TCR phage-display could be used to develop new strategies for isolating TCRs with unique specificity or it could be used to carry out mutagenesis studies on TCR molecules for analyzing their structure-function. We initially selected a TCR from the murine T-cell hybridoma, DO11.10, as our model system, and genetically engineered a three domain **single-chain** TCR (scTCR) linked to the gene p8 protein of the Escherichia coli bacteriophage fd. Immunoblotting studies revealed that (1) E. coli produced a soluble scTCR/p8 fusion protein and (2) the fusion protein was packaged by the phage. Cellular competition assays were performed to evaluate the functionality of the TCR and showed the DO11.10 TCR-bearing phage could significantly inhibit stimulation of DO11.10 T hybridoma cells by competing for binding to immobilized **MHC**/peptide IA(d)/OVA(323-339). Flow cytometric analysis was carried out to evaluate direct binding of DO11.10 TCR-bearing phage onto the surface of cells displaying either IAd containing irrelevant peptide or OVA peptide. The results revealed binding of DO11.10 TCR-bearing phage only on cells expressing IA(d) loaded with OVA peptide showing TCR fine specificity for peptide. To illustrate the generality of TCR phage-display, we also cloned and displayed on phage a second TCR which recognizes a peptide fragment from human tumor suppressor protein p53 restricted by HLA-A2. These findings demonstrate functional TCR can be displayed on bacteriophage potentially leading to the development of novel applications involving TCR phage-display.

L4 ANSWER 2 OF 9 MEDLINE
ACCESSION NUMBER: 97098715 MEDLINE
DOCUMENT NUMBER: 97098715 PubMed ID: 8943392
TITLE: **Single-chain MHC** class II molecules induce T cell activation and apoptosis.
AUTHOR: **Rhode P R**; **Burkhardt M**; **Jiao J**; Siddiqui A H; Huang G P; **Wong H C**
CORPORATE SOURCE: Sunol Molecular Corporation, Miami, FL 33172, USA.
SOURCE: JOURNAL OF IMMUNOLOGY, (1996 Dec 1) 157 (11) 4885-91.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961227

AB **MHC** class II/peptide complexes displayed on the surface of APCs play a pivotal role in initiating specific T cell responses. Evidence is presented here that components of this heterotrimeric complex can be genetically linked into a **single** polypeptide **chain**. Soluble **single-chain** (sc) murine class II IA(d) molecules with and without covalently attached peptides were produced in a recombinant baculovirus-insect cell expression system. Correct conformation of these molecules was verified based on 1) reactivity to Abs directed against conformational epitopes in IA(d) and 2) peptide-specific recognition of the IA(d)/peptide complexes by T cells. Both sc class II molecules loaded the appropriate peptides and sc class II/peptide fusions

were effective in stimulating T cell responses, including cytokine release and apoptosis. Mammalian cells were also found to be capable of expressing functional sc class II molecules on their cell surfaces. The findings reported here open up the possibility of producing large amounts of stable sc class II/peptide fusion molecules for structural characterization and immunotherapeutic applications.

L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:277860 CAPLUS
DOCUMENT NUMBER: 132:320940
TITLE: Polyspecific binding molecules and uses thereof
INVENTOR(S): Weidanz, Jon A.; Card, Kimberlyn; Sherman, Linda A.; Klinman, Norman R.; **Wong, Hing C.**
PATENT ASSIGNEE(S): Sunol Molecular Corporation, USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023087	A1	20000427	WO 1999-US24645	19991021
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1124568	A1	20010822	EP 1999-970601	19991021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-105164P P 19981021
WO 1999-US24645 W 19991021

AB The present invention relates to polyspecific binding mols. and particularly **single-chain** polyspecific binding mols. that include at least one **single-chain** T-cell receptor (s.c.-TCR) covalently linked through a peptide linker sequence to at least one **single-chain** antibody (s.c.-Ab). The polyspecific binding mols. activate immune cells (e.g. cytotoxic T cells, NK cells or macrophages) and kill target cells (e.g. tumor cells or virally infected cells). The polyspecific binding mols. are useful for diagnosis and treatment of cancers and viral infections.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:297317 CAPLUS
DOCUMENT NUMBER: 130:295539
TITLE: Construction of chimeric soluble **MHC** complexes
INVENTOR(S): **Rhode, Peter R.**; Acevedo, Jorge; **Burkhardt, Martin**; **Jiao, Jin-an**; **Wong, Hing C.**
PATENT ASSIGNEE(S): Sunol Molecular Corporation, USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9921572	A1	19990506	WO 1998-US21520	19981013
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6232445	B1	20010515	US 1997-960190	19971029
CA 2307178	AA	19990506	CA 1998-2307178	19981013
AU 9898001	A1	19990517	AU 1998-98001	19981013
EP 1027066	A1	20000816	EP 1998-952256	19981013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002508300	T2	20020319	JP 2000-517730	19981013
US 2002091079	A1	20020711	US 2001-766378	20010119

PRIORITY APPLN. INFO.: US 1997-960190 A 19971029
WO 1998-US21520 W 19981013

AB The authors disclose the construction and expression of sol. **single-chain** (s.c.) **MHC** class II mols. In one aspect, the s.c.-**MHC** class II mols. include a .beta.2 chain modification, e.g., deletion of essentially the entire class II .beta.2 domain. In another aspect, the invention features **single-chain MHC** class II which contain an Ig light chain const. region fragment (CL). The CL fragment allows multimerization of **single-chain** monomers of identical or disparate **MHC** specificity or formation of heteromeric mols. with effector function (e.g., **single-chain** antibodies). In addn., the sol. **MHC** class II mols. can be constructed for exogenous loading of cognate peptides or the requisite peptides can be included in the **single-chain** constructs themselves. In one example, **single-chain** I-Ad mols. were constructed as fusion proteins with T-cell epitopes from either ovalbumin or glycoprotein D of herpes simplex virus. These constructs were shown to stimulate interleukin-2 prodn. by their resp. antigen-specific T-cells. **MHC** complexes of the invention are useful for a variety of applications including: (1) in vitro screens for identification and isolation of peptides that modulate activity of selected T-cells, including peptides that are T cell receptor antagonists and partial agonists, and (2) methods for suppressing or inducing an immune response in a mammal.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:618856 CAPLUS
DOCUMENT NUMBER: 129:229693
TITLE: Fusion proteins comprising bacteriophage coat protein and a **single-chain** T cell receptor
INVENTOR(S): Weidanz, Jon A.; Card, Kimberlyn F.; **Wong, Hing C.**
PATENT ASSIGNEE(S): Sunol Molecular Corporation, USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9839482	A1	19980911	WO 1998-US4274	19980305	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9866856	A1	19980922	AU 1998-66856	19980305	
EP 977886	A1	20000209	EP 1998-908950	19980305	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2001514503	T2	20010911	JP 1998-537984	19980305	
PRIORITY APPLN. INFO.:			US 1997-813781	A 19970307	
			WO 1998-US4274	W 19980305	

AB The present invention relates to novel fusion proteins comprising a bacteriophage coat protein and a **single-chain** T cell receptor and uses of such complexes. In one aspect, the invention relates to sol. fusion protein comprising a bacteriophage coat protein covalently linked to a **single-chain** T cell receptor which comprises a V-.alpha. gene covalently linked to a V-.beta. chain by a peptide linker sequence. The **single-chain** TCR fusion protein typically also includes one or more fused protein tags to help purify the fusion protein from cell components which can accompany it. The TCR used was murine DO11.10 cell TCR which recognizes and binds a chicken ovalbumin peptide spanning amino acids 323-339 in the context of an I-Ad **MHC** class II mol. The sol. fusion proteins of the invention are useful for a variety of applications including: (1) making a bacteriophage library for displaying **single-chain** T cell receptors for use in screens for identification and isolation of ligands that bind **single-chain** T cell receptors, and (2) methods for isolating sol. and fully functional **single-chain** T cell receptors from the fusion proteins. The **single-chain** TCR fusion proteins can be made without performing difficult solubilization, protein refolding or cleaving steps; formation of inclusion bodies in expressing cells is minimal, thereby significantly increasing yields.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:533677 CAPLUS

DOCUMENT NUMBER: 127:204455

TITLE: Preparation and immunomodulatory activity of **single-chain MHC** mols.

INVENTOR(S): **Rhode, Peter R.; Jiao, Jin-An; Burkhardt, Martin; Wong, Hing C.**

PATENT ASSIGNEE(S): Dade International, Inc., USA; Rhode, Peter R.; Jiao, Jin-An; Burkhardt, Martin; Wong, Hing C.

SOURCE: PCT Int. Appl., 216 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

WO 9728191	A1	19970807	WO 1997-US1617	19970130	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,					

RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5869270	A	19990209	US 1996-596387	19960131
CA 2244755	AA	19970807	CA 1997-2244755	19970130
AU 9722538	A1	19970822	AU 1997-22538	19970130
AU 729672	B2	20010208		
EP 877760	A1	19981118	EP 1997-905709	19970130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000515363	T2	20001121	JP 1997-527863	19970130
US 6309645	B1	20011030	US 1998-67615	19980428
US 2002034513	A1	20020321	US 2001-848164	20010503

PRIORITY APPLN. INFO.: US 1996-596387 A 19960131
WO 1997-US1617 W 19970130
US 1998-67615 XX 19980428

AB The present invention relates to novel complexes of major histocompatibility complex (**MHC**) mols. and uses of such complexes. In one aspect, the invention relates to loaded **MHC** complexes that include at least one **MHC** mol. with a peptide-binding groove and a presenting peptide non-covalently linked to the **MHC** protein. In another aspect, the invention features **single chain MHC** class II peptide fusion complexes with a presenting peptide covalently linked to the peptide binding groove of the complex. **MHC** complexes are useful for a variety of applications including: (1) in vitro screens for identification and isolation of peptides that modulate activity of selected T cells, including peptides that are T cell receptor antagonists and partial agonists, and (2) methods for suppressing or inducing an immune response in a mammal.

L4 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:6971 BIOSIS
DOCUMENT NUMBER: PREV200200006971
TITLE: **MHC** molecules and uses thereof.
AUTHOR(S): **Rhode, Peter R.; Jiao, Jin-An (1); Burkhardt, Martin; Wong, Hing C.**
CORPORATE SOURCE: (1) Fort Lauderdale, FL USA
ASSIGNEE: Sunol Molecular Corporation
PATENT INFORMATION: US 6309645 October 30, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 30, 2001) Vol. 1251, No. 5, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB The present invention relates to novel complexes of major histocomability complex (**MHC**) molecules and uses of such complexes. In one aspect, the invention relates to loaded **MHC** complexes that include at least one **MHC** molecule with a peptide-binding groove and a presenting peptide non-covalently linked to the **MHC** protein. In another aspect, the invention features **single chain MHC** class II peptide fusion complexes with a presenting peptide covalently linked to the peptide binding grove of the complex. **MHC** complexes of the invention are useful for a variety of applications including: 1) in vitro screens for identification and isolation of peptides that modulate activity of selected T cells, including peptides that are T cell receptor antagonists and partial agonists, and 2) methods for suppressing or inducing an immune response in a mammal.

L4 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:499745 BIOSIS
DOCUMENT NUMBER: PREV200100499745
TITLE: Soluble **MHC** complexes and methods of use thereof.
AUTHOR(S): **Rhode, Peter R.**; Acevedo, Jorge (1); **Burkhardt, Martin**; **Jiao, Jin-an**; **Wong, Hing C.**
CORPORATE SOURCE: (1) Miami, FL USA
ASSIGNEE: Sunol Molecular Corporation
PATENT INFORMATION: US 6232445 May 15, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (May 15, 2001) Vol. 1246, No. 3, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The present invention relates to novel complexes of major histocompability complex (**MHC**) molecules and uses of such complexes. In one aspect, the invention relates to **single chain** **MHC** class II complexes that include a class II beta2 chain modification, e.g., deletion of essentially the entire class II beta2 chain. In another aspect, the invention features **single** **chain MHC** class II which comprise an immunoglobin constant chain or fragment. Further provided are polyspecific **MHC** complexes comprising at least one **single chain** **MHC** class II molecule. **MHC** complexes of the invention are useful for a variety of applications including: 1) in vitro screens for identification and isolation of peptides that modulate activity of selected T cells, including peptides that are T cell receptor antagonists and partial agonists, and 2) methods for suppressing or inducing an immune response in a mammal.

L4 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:246173 BIOSIS
DOCUMENT NUMBER: PREV199900246173
TITLE: **Single chain MHC** complexes and uses thereof.
AUTHOR(S): **Rhode, P. R.**; **Jiao, J-A.**; **Burkhardt, M.**; **Wong, H. C.**
CORPORATE SOURCE: Miami, Fla. USA
ASSIGNEE: SUNOL MOLECULAR CORPORATION
PATENT INFORMATION: US 5869270 Feb. 9, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 9, 1999) Vol. 1219, No. 2, pp. 1524.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

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L2 47 S L1 AND MHC
L3 22 DUP REM L2 (25 DUPLICATES REMOVED)
L4 9 S L3 AND (SINGLE (1N) CHAIN)

=> s MHC and (class (1N) II) and (single (1N) chain)
L5 128 MHC AND (CLASS (1N) II) AND (SINGLE (1N) CHAIN)

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=> dup rem l6
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L8   10 L7 NOT L4

=> dis l8 1-10 ibib abs

L8   ANSWER 1 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:725480 CAPLUS
DOCUMENT NUMBER: 126:17755
TITLE: **Single-chain MHC**
                         class II molecules induce T cell
                         activation and apoptosis
AUTHOR(S):   Rhode, Peter R.; Burkhardt, Martin; Jiao, Jin-an;
                         Siddiqui, Ayesha H.; Huang, Grace P.; Wong, Hing C.
CORPORATE SOURCE: Sunol Molecular Corporation, Miami, FL, 33172, USA
SOURCE: Journal of Immunology (**1996**), 157(11),
                         4885-4891
                         CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB   **MHC class II**/peptide complexes displayed on
     the surface of APCs play a pivotal role in initiating specific T cell
     responses. Evidence is presented here that components of this
     heterotrimeric complex can be genetically linked into a **single**
     polypeptide **chain**. Sol. **single-chain** (s.c.)
     murine **class II** IAd mols. with and without covalently
     attached peptides were produced in a recombinant baculovirus-insect cell
     expression system. Correct conformation of these mols. was verified based
     on (1) reactivity to Abs directed against conformational epitopes in IAd
     and (2) peptide-specific recognition of the IAd/peptide complexes by T
     cells. Both s.c. **class II** mols. loaded the
     appropriate peptides and s.c. **class Ii**/peptide fusions
     were effective in stimulating T cell responses, including cytokine release
     and apoptosis. Mammalian cells were also capable of expressing functional
     s.c. **class II** mols. on their cell surfaces. These
     findings open up the possibility of producing large amts. of stable s.c.
     class II/peptide fusion mols. for structural
     characterization and immunotherapeutic applications.

L8   ANSWER 2 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:267725 CAPLUS
DOCUMENT NUMBER: 120:267725
TITLE: Intramolecular charge heterogeneity in purified major
                         histocompatibility **class II**
                         .alpha. and .beta. polypeptide chains
AUTHOR(S):   Nag, Bishwajit; Arimilli, Subhashini; Koukis, Bill;

Rhodes, Eric; Baichwal, Varsha; Sharma, Somesh D.
CORPORATE SOURCE: Anergen, Inc., Redwood City, CA, 94063, USA
SOURCE: Journal of Biological Chemistry (**1994**), 269(13), 10061-70
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Major histocompatibility (**MHC**) **class II** antigens are heterodimeric cell surface glycoproteins consisting of an .alpha. and a .beta. chain. Although one-dimensional SDS-PAGE anal. of purified **MHC class II** antigens shows a single diffuse band for each chain, multiple spots of identical mol. size were obsd. for each chain when analyzed by two-dimensional electrophoresis. The basis of this heterogeneity has not been clearly defined and has been predicted partially to be due to glycosylation and/or phosphorylation of the mature protein. To investigate the role of the three N-linked oligosaccharides of the .alpha. and .beta. chains in detg. the isoelec. point of each chain, affinity-purified **MHC class II** antigens from human and rat purified **MHC class II** antigens from human and rat sources were deglycosylated using asparagine amidase. The complete enzymic removal of all three N-linked oligosaccharides were confirmed by SDS-PAGE as well as by four different lectin-linked Western blot analyses. Two-dimensional gel anal. of the deglycosylated mols. shows no difference from the fully glycosylated chains. The authors have expressed truncated forms of the HLA-DR2 chains which lack the transmembrane and cytoplasmically exposed regions in Escherichia coli. Two-dimensional electrophoresis of these **single chains** also reveal multiple banding patterns. The two-dimensional banding patterns described are unaffected by exposure to acidic or basic conditions, increased gel running time in the first dimension, treatment of the proteins with alk. phosphatase to remove any potential phosphorylation, or preincubation in the presence of iodoacetamide. Multiple forms of recombinant .alpha. and .beta. chains were also obsd. in Tris-glycine-urea gels which merged into a single band in the presence of SDS. In addn., partially fractionated bands from preparative isoelec. focusing gels, when refocused, showed an identical no. of multiple spots panning the same range of isoelec. points. These results together suggest that each polypeptide chain of **MHC class II** antigens may exist in multi-conformational forms, and the obsd. charge heterogeneity is independent of glycosylation and phosphorylation of the proteins.

L8 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:252840 CAPLUS
DOCUMENT NUMBER: 118:252840
TITLE: Stimulation of T cells by antigenic peptide complexed with isolated chains of major histocompatibility complex **class II** molecules
AUTHOR(S): Nag, Bishwajit; Wada, H. Garrett; Deshpande, Shrikant V.; Passmore, David; Kendrick, Teresa; Sharma, Somesh D.; Clark, Brian R.; McConnell, Harden M.
CORPORATE SOURCE: Anergen Inc., Redwood City, CA, 94063, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1993**), 90(4), 1604-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Major histocompatibility complex (**MHC**) **class II** mols. are heterodimeric glycoproteins with one .alpha. and one .beta. polypeptide chain of similar mol. size. In this report, the binding is described of an acetylated N-terminal peptide of myelin basic protein, [Ala4]MBP-(1-14), to purified individual .alpha. and .beta. chains of murine I-Ak mols. Purified complexes of isolated **single**

chains and antigenic peptide bind to cloned T cells restricted by I-Ak and [Ala4]MBP-(1-14) tetradecapeptide. The binding is blocked by .alpha./.beta. anti-T-cell receptor (TCR) monoclonal antibody. Cell triggering, as measured by an increase in extracellular acidification rate, is obsd. when cloned T cells are exposed to purified complexes of isolated chains and antigenic peptide. This increase in the extracellular acidification rate is antigen specific and **MHC**-restricted, as chains alone or irrelevant chain-peptide complexes do not trigger an increase in the metabolic acidification rate. These results together demonstrate that in vitro cloned T cells are triggered by complexes of specific antigenic peptides and isolated individual chains of their cognate **MHC** proteins.

L8 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:20526 CAPLUS
DOCUMENT NUMBER: 118:20526
TITLE: Preparative-scale purification and characterization of **MHC class II** monomers
AUTHOR(S): Passmore, David; Kopa, David; Nag, Bishwajit
CORPORATE SOURCE: Anergen Inc., Redwood City, CA, 94063, USA
SOURCE: Journal of Immunological Methods (**1992**), 155(2), 193-200
CODEN: JIMMBG; ISSN: 0022-1759
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **MHC class II** mol. is a heterodimeric glycoprotein consisting of one .alpha. and one .beta. polypeptide chain of almost identical mol. size. It is known that isolated monomers of murine **MHC** II mols. are capable of binding antigenic peptides. In addn., preliminary results indicate that isolated **single chain** -peptide complexes of murine **MHC class II** mols. are capable of stimulating cloned T cells in an antigen specific manner. This report describes micro-preparative and preparative continuous flow electrophoresis methods by which milligram quantities of **MHC** II subunits can be purified. An optimal condition for the dissocn. of heterodimeric **MHC** II into .alpha. and .beta. monomers was identified, and sepn. of human HLA DR2 and murine IAS monomers was accomplished. Both methods offer the resolving power of gel electrophoresis with the convenience of continuous sample elution. Purified **MHC** II subunits obtained by these methods were tested for their ability to bind antigenic peptides. Results presented in this study indicate that monomeric subunits of both human HLA-DR2 and murine IAS are equally active in specific binding of antigenic peptides like the native heterodimer.

L8 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:249808 CAPLUS
DOCUMENT NUMBER: 116:249808
TITLE: Single base pair substitutions within the HLA-DRA gene promoter separate the functions of the X1 and X2 boxes
AUTHOR(S): Sloan, John H.; Hasegawa, Susan L.; Boss, Jeremy M.
CORPORATE SOURCE: Sch. Med., Emory Univ., Atlanta, GA, 30322, USA
SOURCE: Journal of Immunology (**1992**), 148(8), 2591-9
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **class II MHC** genes are expressed on the surfaces of B cells, activated T cells, and macrophages and may be induced in other cell types by IFN-.gamma.. The control of **class II** gene expression has been shown to be mediated by a series of conserved cis-acting sequences (W, XI, X2, and Y boxes) located immediately 5' to the genes. Although these sequences are conserved, the bp that are important for transcriptional regulation have yet to be identified. To address this issue with regard to the **MHC** gene

HLA-DRA, a series of single bp substitutions spanning the conserved upstream sequences was created and analyzed for their effects on transcription in both B cells and IFN-.gamma.-treated fibroblasts. In addn., the effects of X1 and X2 box mutations on DNA/protein interactions were examd. and compared to the transcriptional data. The results of these studies show that each of the conserved elements participate in maximal expression in B cells and that W, X1, and X2 boxes are important for IFN-.gamma. induction and expression in fibroblasts. Interestingly, some of the bp changes that altered B cell expression did not alter expression and IFN-.gamma. induction in fibroblasts, suggesting that different or altered factors control the expression of these genes in the different cell types. Mutant templates designed to eliminate the binding of X1- and X2-specific DNA binding proteins in vivo suggest that these elements and their factors may interact to promote transcription.

L8 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:74910 CAPLUS
DOCUMENT NUMBER: 112:74910
TITLE: Structural analysis of the interaction of apamin with Ia and its recognition by Ad- or Ab-restricted mouse T cells
AUTHOR(S): Regnier-Vigouroux, Anne; Ceard, Brigitte; Van Rietschoten, Jurphaas; Granier, Claude; Pierres, Michel
CORPORATE SOURCE: Cent. Immunol., Marseille, 13288, Fr.
SOURCE: Journal of Immunology (**1989**), 143(10), 3167-74
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Apamin is a **single-chain**, disulfide-bonded, 18-amino acid peptide that elicits mouse T cell responses when presented by cells expressing syngeneic Ad or Ab **class II MHC** mols. To seek further information on the sites through which this peptide interacts with Ia and/or TCR, a panel of Ad- or Ab-restricted, apamin-specific THC was used to probe the antigenicity of a series of synthetic apamin analogs. These included peptides either truncated at the N terminus, or substituted by Ala at position 2, 4, 6, 7, 8, or 10. Anal. of THC responses to apamin analogs and use of the latter in competition assays for peptide presentation revealed the following: 1) optimal apamin T cell recognition critically involved Lys4, Ala5, Pro6, Glu7, and Leu10. The role of these residues in either Ia or TCR binding regions was dependent upon the restricting Ia mols. at play. Thus, Lys4, Glu7, and Leu10 were TCR-binding residues in both Ad- and Ab-apamin complexes, whereas Lys4 participated in apamin/Ab but not, or to a marginal extent, in apamin/Ad interaction. Furthermore, Pro6 was assocd. either with an Ia contact region or a TCR interaction site when apamin was presented by Ab or Ad mols., resp. Unfolded apamin and the unrelated chicken OVA323-339 peptide were bound to the same, or closely related site(s) of Ad, as shown by their ability to compete reciprocally for recognition by appropriate Ad-restricted THC. Four distinct TCR V.beta. genes (V.beta.2, V.beta.4, V.beta.6, and V.beta.8) were found to be used in this panel of 16 apamin-specific THC. Thus, apamin interacts with Ad or TCR through a motif resembling other .beta.-sheeted, Ad-binding sequences; however, based on the spacing of the crit. residues (i.e., 4, 7, and 10), the possibility exists that apamin processing permits the folding of this sequence into an .alpha.-helix.

L8 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:4420 CAPLUS
DOCUMENT NUMBER: 108:4420
TITLE: Supplementary characteristics of anti-**MHC class II** monoclonal antibodies elicited by an ALL cell line: immunofluorescence

cytofluorometry, C-dependent cytotoxicity, two-dimensional analysis of antigen

AUTHOR(S): Chorvath, B.; Duraj, J.; Sedlak, J.; Pleskova, I.; Munozova, H.; Buc, M.

CORPORATE SOURCE: Cancer Res. Inst., Slovak Acad. Sci., Bratislava, 812 32, Czech.

SOURCE: Neoplasma (**1987**), 34(4), 417-25
CODEN: NEOLA4; ISSN: 0028-2685

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Monoclonal antibodies directed to major histocompatibility complex (**MHC**) **class II** antigen(s) were elicited by immunization with a non-T, non-B acute lymphocytic leukemia cell line. The antibodies were characterized by various immunochem. techniques, including complement (C-)-dependent cytotoxicity. Patterns of these immunol. reactivities, as well as 2-dimensional radioimmunopptn. patterns (acidic heavy chain p35 and basic light chain p30) of antigens recognized by these antibodies confirm their anti-**MHC class II** specificity. One of these antibodies (braFB6; IgG2b) displayed identical pattern of reaction with cell lines and cell types as do the typical anti-**MHC class II** antibodies, but immunopptd. only a **single chain** p30 radioiodinated cell surface protein (which has a 2-dimensional pattern close to the .beta.-chain of **MHC class II** DR antigen). Thus, the ability of the braFB6 monoclonal antibody to recognize a nonpolymorphic determinant of DP-**MHC class II** antigen is shown.

L8 ANSWER 8 OF 10 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94248831 EMBASE

DOCUMENT NUMBER: 1994248831

TITLE: [Graft rejection across transgene-encoded **MHC class II** molecules].
REJETS DE GREFFE INDUITS PAR LES MOLECULES DE CLASSE II DU CMH: ETUDE PAR TRANSGENESE.

AUTHOR: Rosay P.; Hergueux J.; Benoist C.; Mathis D.

CORPORATE SOURCE: Lab. de Genetique Moleculaire des, Eucaryotes, CNRS, 11, Rue Humann,67085 Strasbourg, France

SOURCE: Comptes Rendus de l'Academie des Sciences - Serie III, (**1994**) 317/7 (639-643).
ISSN: 0764-4469 CODEN: CRASEV

COUNTRY: France

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: French; English

AB To investigate the capacity of **class II** gene products of the major histocompatibility complex to serve as targets for allograft rejection, we have used lines of transgenic mice which express such genes on a common genetic background. These lines allow us to test the function of single **class II** molecules, or of **single chains** of the **class II** heterodimers, in graft rejection or tolerance induction. Our data show that some **class II** molecules (A.alpha., A.beta.) can induce very efficient rejection, while others are relatively inert (E), and that tolerance induction requires matching for both chains of the target **class II** heterodimers.

L8 ANSWER 9 OF 10 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 83127926 EMBASE

DOCUMENT NUMBER: 1983127926

TITLE: In vitro correlate for a clonal deletion mechanism of immune response gene-controlled on responsiveness.

AUTHOR: Ishii N.; Nagy Z.A.; Klein J.

CORPORATE SOURCE: Abt. Immungenet., Max Planck Inst. Biol., 7400 Tubingen, Germany
SOURCE: Journal of Experimental Medicine, (**1983**) 157/3 (998-1005).
CODEN: JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
051 Leprosy and other Mycobacterial Diseases
022 Human Genetics
LANGUAGE: English
AB We used T cell-antigen-presenting cell (APC) combinations from two pairs of recombinant mouse strains, B10.A(4R)-B10.A(2R) and B10.S(7R)-B10.S(9R) (abbreviated 4R, 2R, 7R, 9R, respectively), which differ from each other only in the nonexpression vs. expression of cell-surface E molecules, to study the mechanism of the Ir gene-controlled (E-restricted) response to the terpolymer poly(glu51lys34tyr15) (GLT). No response to GLT occurred when the APC were from E-nonexpressor strains 4R and 7R. When APC from E-expressor strains were used and alloreactivity against the incompatible E molecules was removed by BUdR + light treatment, 7R T cells responded to GLT presented by 9R APC, but 4R T cells failed to respond to GLT presented by 2R APC. However, 4R T cells mounted a proliferative response to GLT presented by fully allogeneic 5R or 9R APC. The latter response was completely abolished by the depletion of cells alloreactive against 2R and 5R or 2R and 9R. Since removal of alloreactivity against 5R plus 9R did not affect the response of 4R T cells to GLT presented by either 5R or 9R cells, we conclude that the 4R T cells generated in response to GLT cross-react with the additional incompatibility presented by 2R cells, that is, the E(k).beta. chain. In contrast, 7R T cells recognizing GLT presented by 9R APC do not cross-react with E(k).beta.. These results demonstrate that 'blind spots' in the T cell repertoire produced by depletion of cells alloreactive against a **single chain** of a **class II MHC** molecule can render a strain nonresponsive to a synthetic polypeptide antigen, and that this nonresponsiveness corresponds to that attributed to the **MHC** linked Ir genes.

L8 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:139350 BIOSIS
DOCUMENT NUMBER: PREV199799438553
TITLE: Single-strand conformation polymorphism analysis of the second exon of a **MHC class II** DRB gene in sheep.
AUTHOR(S): Jugo, B.; Martinez, N.; Estomba, A.; Vicario, A.
CORPORATE SOURCE: Dep. Anim. Biol. and Genetics, Fac. Sci., Univ. Basque Country, Basque Country Spain
SOURCE: Animal Genetics, (1996) Vol. 27, No. SUPPL. 2, pp. 53-54.
Meeting Info.: 25th International Conference on Animal Genetics Tours, France July 21-25, 1996
ISSN: 0268-9146.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

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(FILE 'HOME' ENTERED AT 15:54:07 ON 22 NOV 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 15:54:18 ON 22 NOV 2002
L1 9889 S RHODE P?/AU OR JIAO J?/AU OR BURKHARDT ?/AU OR WONG H?/AU
L2 47 S L1 AND MHC
L3 22 DUP REM L2 (25 DUPLICATES REMOVED)
L4 9 S L3 AND (SINGLE (1N) CHAIN)
L5 128 S MHC AND (CLASS (1N) II) AND (SINGLE (1N) CHAIN)